Letters to the Editor

Treatment of severe Raynaud’s phenomenon with bosentan in a patient with systemic sclerosis

Sir, Raynaud’s phenomenon is characterized by recurrent episodes of vasospasm most commonly occurring in the hands and feet. It is a manifestation of the widespread vascular involvement that occurs in systemic sclerosis [1]. Digital ischaemic and necrotic lesions are a frequent complication, with an estimated frequency of 30–40% [2]. Recent studies indicate that bosentan prevents the occurrence of new digital ulcers [3] and may promote actual healing [4, 5]. The effects of bosentan on peripheral blood flow, circulating endothelial cells (CD146+), and progenitor cells (CD34+) involved in vessel repair, have not been reported.

We examined and treated a 42-yr-old woman with SCL-70-negative systemic sclerosis, early interstitial pulmonary fibrosis and an estimated pulmonary arterial pressure of 37 mmHg. Over the space of 1 yr she developed skin thickening, Raynaud’s phenomenon, and then finger tip ulcers, pulp space loss and gangrene. Angiograms of the right hand showed severe vasculopathy with abrupt termination of nearly all digital arteries, the most severely affected being the index and ring fingers. The condition did not respond to calcium channel blockers, nitroglycerine or sympathetic blockade. Epoprostenol or equivalent medications were not available. She was begun on bosentan initially at 37.5 mg twice per day, her initial tolerance level, and then at 62.5 mg twice per day a month later, then 125 mg twice per day. On this regimen there was dramatic and sustained improvement, which began to occur even on the small initial doses of bosentan.

![Fig. 1. Effects of bosentan on peripheral blood flow and ulcer healing before (L) and on bosentan (R).](image-url)
Small-vessel blood flow measured by laser Doppler fluximetry (Moore Inc, Wilmington, Delaware, USA) showed improvement (Fig. 1a, right vs left). The gangrenous areas healed within a month (Fig. 1b, right vs left). The vasodilator changes were not sustained over time, but the vessels did show increased responses to a warm and cold challenge (Fig. 2b). Circulating numbers of CD146 cells, a population of mainly endothelial cells, showed a dramatic drop over time, suggesting a reduction in vascular injury. There was a concomitant increase in circulating CD34 cells, a population of stem cells which contains endothelial progenitors or angioblasts (Fig. 2a).

In this patient, bosentan appeared to have had a beneficial effect in healing of the gangrenous lesions of severe Raynaud’s phenomenon. There was a concomitant decrease in pain and improvement in function, which was sustained. It also improved peripheral blood flow and vessel responsiveness. Our finding of a significant decrease in circulating CD146 cell levels with a concomitant rise in CD34 cell levels suggests a decrease in endothelial damage and an increase in circulating stem cells involved in vessel repair. Circulating endothelial cells have been shown to be a marker of vascular damage in scleroderma and other conditions [6–9]. Furthermore, CD34 cells contain a fraction of angioblasts which have the ability to repair damaged vasculature [10]. This case suggests that further study of the effect of bosentan in vascular healing and possibly remodelling are needed.

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Pneumococcal and influenza vaccination in patients with rheumatic conditions and receiving DMARD therapy

Sir, It was interesting to read your editorial ‘Vaccinate your immunocompromised patients!’ [1] and we would like to outline an audit performed at Wrightington Hospital, UK, which highlights this problem. *Streptococcus pneumoniae*, the most common cause of adult community-acquired pneumonia, has an annual incidence rate of between 10 and 100 cases per 100,000 population [2]. The annual incidence of influenza infection varies; however, it has the propensity to cause epidemics affecting up to 15% of the population [3]. In the UK, the Department of Health runs campaigns to encourage yearly vaccination against influenza and immunization against pneumococcus in those aged ≥65 and those in ‘at risk’ groups <65 years of age [4, 5]. However, much of the promotional material available is aimed at those >65 yr of age [6]. Furthermore, funding is based on the >65 population covered by a given primary care trust.

Patients with rheumatic disease represent an ‘at risk’ group as a result of immunosuppressive disease modifying anti-rheumatic drug (DMARD) therapy that increases their susceptibility to infection. As such, they should be immunized against pneumococcal and influenza infection. We performed an audit to assess the level of pneumonia and influenza vaccine awareness and uptake in 100 patients treated with DMARDs (e.g. methotrexate, azathioprine and cyclosporine) attending our unit between